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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,822	07/22/2003	Shuichi Mizuno	3831.09	7790

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EXAMINER	
NAFF, DAVID M	
ART UNIT	**PAPER NUMBER**
1657	

DATE MAILED: 11/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,822	MIZUNO ET AL.	
	Examiner	Art Unit	
	David M. Naff	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-9 and 21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7-9 and 21-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/3/03, 3/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A response of 8/2/06 to a restriction requirement of 6/29/06 amended claims 2, 5, 7-9, added new claims 21-30, canceled claims 1, 6 and 10-20, and elected with traverse Group I claims 1-9.

Since nonelected claims 10-20 have been canceled, the traverse is moot.

Claims examined on the merits are 2-5, 7-9 and 21-30, which are all claims in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5, 7-9 and 21-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to disclose a method as required by claim 21 of preparing a neo-cartilage construct comprising isolated chondrocytes seeded into a support matrix containing a plurality of pores, and then subjecting the construct to conditions of static, constant or cyclic hydrostatic pressure, atmospheric pressure or non-

pressure conditions. Chondrocytes seeded into a matrix will not be a neo-cartilage construct since cartilage has not been produced. The neo-cartilage construct results only after the chondrocytes seeded in the support have been treated as disclosed in the specification at page 38, lines 19-32 and page 39, lines 7-11 by using hydrostatic pressure at a certain pressure and freguency and time above atmospheric, perfusion at a certain flow rate for a certain time and a resting period at atmospheric pressure for certain times. Claim 21 does not require using any pressure above atmospheric and any resting period at atmospheric pressure due to the claim encompassing atmospheric pressure or non-pressure conditions, conditions for applying pressure of zero MPa and zero time, and zero time for applying a resting period. The claim does not require perfusion that the specification indicates is required to produce the neo-cartilage construct.

The specification fails to disclose a gel as being alternative to specific gels as in claims 22 (line 2), 26 (line 3) and 27 (line 3). As disclosed in the specification, the specific gels are the gel to be used, and are not alternative to a gel.

The specification fails to disclose a honeycomb and honeycomb lattice being alternatives as in claim 22 (line 4). When a honeycomb lattice is present, this is the honeycomb, and not the alternative of a honeycomb.

The specification fails to disclose periods required in claims 28 and 30 of "4 hours per day" and "20 hours per day". Additionally, a

time of "about 7 days" for a resting period as required in claims 28 and 30 is not found in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 7-9 and 21-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Reciting in claim 21 "zero MPa to about 10 MPa", "zero to about 24 hours" and "zero to about 24 hours per day" makes unclear as to conditions required since when zero the condition recited is not present. Due to the recital of "zero", claim 21 does not require any pressure, any frequency and any resting period. This also applies to reciting "zero" in claim 9, and this claim does not require any pressure and resting period for treating the neo-cartilage construct.

When the resting period precedes the hydrostatic pressure as an alternative to following the hydrostatic pressure in claims 9 and 21, it is not seen how the period can be a resting period since no hydrostatic pressure has been applied which can be removed to provide a resting.

In line 7 of claim 21, the difference in static and constant hydrostatic pressure is uncertain. A static pressure would appear to be a constant pressure, or the converse.

Bridging lines 8 and 9 of claim 21, conditions are uncertain that are "non-pressure" and alternative to hydrostatic and atmospheric pressure. The specification fails to describe non-pressure conditions.

In line 4 of claim 21 and where recited in other claims, "neo-cartilage construct" is uncertain as to meaning and scope. It is uncertain how "neo" defines the construct, and how one would know when a construct is neo and not neo.

Step b) of claim 21 is confusing by requiring implanting the construct into injured or damaged articular cartilage, whereas the claim preamble requires damaged, injured, diseased or aged articular cartilage. Step b) should be consistent with the claim preamble.

In claim 5, the meaning and scope of "superficial cartilage layer" is uncertain. How "superficial" defines the cartilage layer is unclear. Additionally, where does this layer exist relative to the top sealant and construct in the lesion. Furthermore, claim 5 is confusing as to steps performed by not setting forth clear, distinct and positive method steps.

Claim 7 is unclear in lines 4-7 as to the components of the Markush group that are contained and not contained by the cell-contracted collagen. Is glycoprotein the last component, or are other components contained by the contracted collagen. It is suggested

"cell-contracted collagen containing proteoglycan, glycosaminoglycan or glycoprotein" be changed to "cell-contracted collagen containing a material selected from the group consisting of proteoglycan, glycosaminoglycan and glycoprotein,".

To be clear, claim 9, line 4, should change "hydrostatic cyclic pressure" to --- cyclic hydrostatic pressure --- to be consistent with claim 21. Additionally, "constant pressure" line 6 of claim 9 should be changed to --- constant hydrostatic pressure --- since the constant pressure in claim 21 is hydrostatic pressure. Claim 9 is dependent on claim 21 via claim 8, and the constant pressure in claim 9 must be hydrostatic pressure since claim 9 cannot broaden claim 21 as to constant pressure required.

In line 12 of claim 9, the perfusion flow rate is unclear by reciting "μL" instead of "μL/min" as in claim 8.

In line 8, claim 9 is unclear as to whether the pressure applied for 7-28 days is the hydrostatic cyclic pressure or the constant pressure previously required. If intended to be the constant pressure, this pressure can be zero, and when zero it is uncertain how pressure can be applied for 7-28 days.

In line 2 of claim 29, "TRGH" should be in parenthesis and preceded by the full name to be clear as to the meaning of the abbreviation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 21 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Smith et al (6,528,052 B1).

The claims are drawn to a method for repairing and restoration of damaged, injured, diseased or aged articular cartilage to form a functional hyaline cartilage. The method comprises preparing a neo-cartilage construct comprising isolated chondrocytes seeded into a three-dimensional support matrix containing a plurality of pores, and subjecting the construct to a static, constant or cyclic hydrostatic pressure, atmospheric pressure or non-pressure conditions, and implanting the construct into the injured or damaged articular cartilage or into a lesion in the articular cartilage.

Smith et al disclose a method for *in vivo*, *ex vivo* or *in vitro* repair and regeneration of cartilage. The cartilage can be articular cartilage (col 1, line 42). *In* vitro treatment is performed by obtaining cartilage cells from cartilage, applying an interval loading regiment while culturing the cartilage cells in suspension within a scaffold/support, and implanting the resultant tissue or cells into a patient (col 9, lines 23-30, and col 11, lines 5-9). The interval

loading regiment involves treatment of cartilage or cartilage cells by using conditions of intermittent application of periods of hydrostatic pressure followed by periods of recovery (col 4, lines 25-31, and col 7, line 30 to col 8, line 8). The recovery period can be at atmospheric or low constant pressure (col 7, lines 48-50).

Smith et al disclose a method for repairing and regenerating cartilage that is the same as presently claimed. The cartilage regenerated will inherently be functional hyaline cartilage.

The presently claimed invention is not disclosed in parent application 10/104,677, and the parent application cannot be relied on for a priority date earlier than the filing date the present application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of

each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al in view of Vacanti et al (6,027,744).

The claims are drawn to the support matrix being prepared from materials including a polymeric thermo-reversible gelling hydrogel (THGH).

Smith et al is described above.

Vacanti et al disclose generating new tissue in a patient by providing a hydrogel containing tissue precursor cells in a support structure, and implanting the hydrogel-containing support structure in a patient (col 1, lines 34-50). The cells can be chondrocytes (col 2, line 64), and the tissue produced can be cartilage (col 4, line 50). The hydrogel can be a reverse-thermosensitive copolymer gel that is liquid below a certain temperature, and which solidifies above a certain temperature (col 14, lines 35-45). The support structure can be formed of polyglycolic fibers (col 12, line 63). Using a hydrogel in a support structure improves the quality of new tissue growth, and the range of tissue shapes and structures that can be grown. In addition, the hydrogel allows diffusion of nutrients and waste products to and away from the cells, which promotes tissue growth (col 1, lines 51-62).

It would have been obvious to use as the scaffold/support of Smith et al a hydrogel in support structure as disclosed by Vacanti et al to obtain its advantages of improved the quality of new tissue growth, range of tissue shapes and structures that can be grown, and allowing diffusion of nutrients and waste products to promote tissue growth.

Claim Rejections - 35 USC § 103

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al in view of Nevo et al (6,632,651 B1).

Claim 8 requires the matrix seeded with chondrocytes to be perfused with a medium at a flow rate from about 1 μL/min to about 500 μL/min.

Smith et al is described above.

Nevo et al disclose perfusing cells with a medium to maintain viability and growth prior to implanting (col 2, lines 8-15 and col 8, lines 41-43).

It would have been obvious to perfuse cells in the scaffold/support of Smith et al with culture medium to maintain viability and growth of the cells as suggested by Nevo et al. Selecting a preferred flow rate of about 1 μL/min to about 500 μL/min would have been obvious to maintain preferred optimum viability and growth of cells.

Claim Rejections - 35 USC § 103

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claim 8 above, and further in view of Hungerford et al (6,378,527 B1).

The claim requires specific conditions of pressure and frequency for using hydrostatic cyclic pressure, and carrying out perfusion at a flow rate in a range of about 5 μL to about 50 μL and in the presence of about 2% to about 5% oxygen.

Hungerford et al disclose that using a low oxygen level of about 5% when culturing chondrocytes seeded on a scaffold results in enhanced expression of collagen type II and aggrecan, as well as helping maintain chondrocyte phenotype (col 24, lines 14-23).

It would have been obvious to use a low oxygen level of about 5% when culturing chondrocytes in the scaffold/support of Smith et al to obtain enhanced expression of collagen type II and aggrecan, as well as helping maintain chondrocyte phenotype as suggested by Hungerford et al. The pressure and frequency for hydrostatic cyclic pressure of the claim would have been obvious from the pressure and frequency disclosed by Smith et al. The perfusion flow rate would have been obvious for reasons set forth above. Since the constant pressure and resting period claimed can be zero, the claim does not require a constant pressure and resting period.

Claim Rejections - 35 USC § 103

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al in view of Wise et al (American Surgeon) and Rhee et

al (5,475,052), and if necessary in further view of Rhee et al (5,565,519).

The claim requires applying a layer of top sealant over the cartilage implanted into a lesion.

Smith et al is described above.

Wise et al disclose using a collagen-polyethylene glycol sealant to seal leaks after liver transplantation.

Rhee et al ('052) disclose using a collagen-polyethylene glycol matrix (cols 15-17, and col 20, line 60 to col 23, line 67) for implant applications.

Rhee et al ('519) disclose using a collagen-polyethylene glycol conjugate for ophthalmic applications (cols 9-20).

It would have been obvious to seal a defect after implanting cartilage tissue in a defect as disclosed by Smith et al using a collagen-polyethylene glycol sealant as suggested by Wise et al using this sealant and Rhee et al using a collagen-polyethylene glycol matrix for implant applications. It would have been obvious that sealing the defect after implanting will be advantageous to prevent contamination and infection at the site of the defect. If needed, Rhee et al ('519) would have further suggested using a collagen-polyethylene glycol sealant from disclosing using a collagen-polyethylene glycol conjugate for ophthalmic applications. Formation of a superficial cartilage layer will be inherent when the defect containing the sealed implanted construct heals.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 7-9 and 21-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,949,252 B2 or claims 1-20 of U.S. Patent No. 6,528,052 B1 in view of Wise et al and Rhee et al ('052), and if necessary in further view of Rhee et al ('519).

For the type of reasons set forth in the 103 rejection, it would have been obvious to seal a defect after implanting the cartilage construct of the claims of the patents using a sealant as suggested by Wise et al and Rhee et al ('052), and if needed Rhee et al ('519). Formation of a superficial cartilage layer will be inherent when the defect containing the sealed implanted construct heals.

Double Patenting

Claims 2-5, 7-9 and 21-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-9, 12-17, 19 and 21-28 of copending Application No. 10/626,459. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed method for repair and regeneration of articulator cartilage using a top sealant, or top and bottom sealants, would have been obvious from the claimed method of the copending application for repairing articular cartilage using top and bottom sealants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Double Patenting

Claims 2, 7-9 and 21-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-42 of copending Application No. 10/625,245 or claims 1-29 of copending Application No. 11/413,419 in view of Wise et al and Rhee et al ('052), and if necessary in further view of Rhee et al ('519).

For the type of reasons set forth in the 103 rejection, it would have been obvious to seal a defect after implanting the cartilage construct of the claims of the copending applications using a sealant as suggested by Wise et al and Rhee et al ('052), and if needed Rhee et al ('519). Formation of a superficial cartilage layer will be

inherent when the defect containing the sealed implanted construct heals.

This is a provisional obviousness-type double patenting rejection.

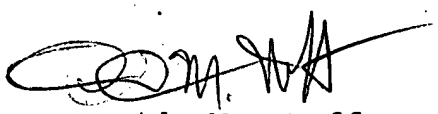
Conclusion

Claims 3-5 and 24-30 are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner

Art Unit 1651

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